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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,105	09/10/2004	Takayuki Fujii	Q83547	2105

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EXAMINER

MARTIN, PAUL C

ART UNIT	PAPER NUMBER
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1655

DATE MAILED: 04/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/507,105		FUJII, TAKAYUKI	
	Examiner		Art Unit	
	Paul C. Martin		1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>02/10/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

All objections and rejections not repeated in the instant Action have been withdrawn due to Applicant's response to the previous Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-13, 15-20 and 21-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Madappally et al. (4,241,179).

This rejection is maintained for reasons of record set forth in the paper mailed 08/29/05, repeated below (extended to new claims to take into consideration applicant's amendment to the claim filed 01/30/06).

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Madappally et al. teaches a two-reagent system for measuring the activity of glutamate pyruvate transaminase, also known as alanine aminotransferase. The first reagent contained at least nicotinamide adenine dinucleotide, lactate dehydrogenase, and L-alanine. (Column 6, Table 1) The second reagent contained at least, a substance having an activity of inhibiting lactate dehydrogenase activity i.e., oxalic and oxamic acid or salts thereof, and alpha-ketoglutarate, also known as 2-oxoglutaric acid (Column 6, Table 2).

Madappally et al. teaches a method for measuring the activity of alanine aminotransferase by bringing a sample to be analyzed into contact with L-alanine, 2-oxoglutaric acid, lactate dehydrogenase in a final concentration of 200-500 U/L, nicotinamide adenine dinucleotide, and substances having an activity of inhibiting lactate dehydrogenase activity i.e., oxamic and oxalic acid, (Column 4, Lines 62-68, Column 5, Lines 1-8, Column 6 Table 1) and measuring the increased/decreased amount of oxidized/reduced nicotinamide adenine dinucleotide generated. (Column 1, Lines 45-55)

Wherein claim 19 recites "same reagent-component", this phrase is not specifically defined in the specification. Therefore, it is given its broadest possible interpretation, within reason, in terms of examination.

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It is deemed that because all of the components were combined with the sample, that this combination taught by Madappally *et al* of: sample, lactate dehydrogenase, lactate dehydrogenase inhibitor, L-alanine, 2-oxoglutaric acid, and oxidized nicotinamide adenine dinucleotide anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Madappally *et al*.

Madappally *et al*. teaches a two-reagent system for measuring the activity of glutamate pyruvate transaminase, also known as alanine aminotransferase. The first reagent contained at least nicotinamide adenine dinucleotide, lactate dehydrogenase, and L-alanine. The second reagent contained at least, a substance having an activity of inhibiting lactate dehydrogenase activity; oxalic and oxamic acid or salts thereof, and alpha-ketoglutarate, also known as 2-oxoglutaric acid. (Column 4, Lines 62-68, Column 5, Lines 1-8)

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Madappally *et al.* teaches a method for measuring the activity of alanine aminotransferase by bringing a sample to be analyzed into contact with L-alanine, 2-oxoglutaric acid, lactate dehydrogenase in a final concentration of 200-500 U/L, nicotinamide adenine dinucleotide, and substances having an activity of inhibiting lactate dehydrogenase activity; oxamic and oxalic acid. (Column 4, Lines 62-68, Column 5, Lines 1-8, Column 6 Table 1)

Madappally does not teach the use of a concentration of oxamic acid or salt thereof, from 0.005 to 5 mmol/L as a final concentration in a measuring system.

One of ordinary skill in the art would have been motivated to use the following ratios because the artisan would have recognized that these proportions were conventional in the art at the time and that the artisan would have had a reasonable expectation of success using these ratios.

Madappally *et al.* teaches the use of a concentration of oxamic acid at 10-30mmol/L per 200-500U/L of lactate dehydrogenase. Applicants' claims call for use of a concentration of oxamic acid (or salt thereof) at 0.005 to 5mmol/L per 100U/L or more of lactate dehydrogenase. On average, applicants' ratio of oxamic acid to lactate dehydrogenase is about 1:20. Madappally *et al.* teach an average ratio of oxamic acid to lactate dehydrogenase of about 1:17.5.

The MPEP states that: "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" as well as "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." In re Peterson, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003)".

Variations among the concentrations concerning enzymatic assays are conventional in the art. It is noted, as stated above, that the ratios disclosed by Madappally et al. is a narrower range that is very close to the claimed range. Optimization of variables is considered routine experimentation, well within the purview of the ordinary artisan at the time of the invention.

Applicant's arguments filed 01/30/06 have been fully considered but they are not deemed to be persuasive.

Response to Arguments

The Applicant argues that the use of “a substance having an activity of inhibiting a lactate dehydrogenase activity” is an improvement to a known method for measuring alanine aminotransferase activity. The Applicant claims the unexpected results of suppressed increased initial absorbance, more accurate measurement of alanine aminotransferase activity and a stabilizing effect on lactate dehydrogenase. Applicant discloses that the reasons for the unexpected results have not been fully determined but offers a hypothesis as a possible explanation. Applicant argues that the use of an LD inhibitor is neither disclosed or suggested by Madapally, that there is no motivation based on the teachings of Madapally to suggest the use of an LD inhibitor to one of ordinary skill in the art, and that the unexpected results are neither disclosed or suggested by Madapally.

The use of lactate dehydrogenase inhibiting substances are disclosed several times in the disclosure of Madapally for use in a method for measuring alanine aminotransferase (Column 4, Lines 23-33 and Column 5, Lines 5-12 and Claims 1 and 4). Madapally discloses that the purpose of their **improved** method is the elimination of initial color development (which will increase initial absorbance) allowing for accurate determination of alanine aminotransferase activity (Column 3, Lines 48-57).

As Madapally fully anticipates the claimed invention it is deemed that the stabilizing effect on LD activity would likewise be inherent to the method of Madapally. Applicant's claim of unexpected results without proof that the results are due in fact to the improvements claimed is not found to be convincing.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-15, 17-20 and 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Amended Claims 12 and 17 contain the language "wherein the concentration of the substance in the measuring system is a concentration *exhibiting* the lactate dehydrogenase activity" while claims dependent on those claims only refer to a "substance having an activity of *inhibiting* a lactate dehydrogenase activity". It is unclear whether the Applicant is referring to a substance which has lactate dehydrogenase activity or can inhibit the activity of lactate dehydrogenase.

This is a new rejection necessitated by the Applicant's amendment filed 01/30/06.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Paul Martin
Examiner
Art Unit 1655

04/01/06

PATRICIA LEITH
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Patricia Leith', with a large, stylized flourish extending from the end of the signature.